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GORDON RESEARCH CONFERENCE ON DRUG CARRIERS IN BIOLOGY
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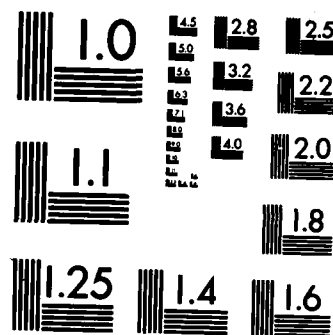
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GORDON RESEARCH CONFERENCE ON DRUG CARRIERS IN BIOLOGY
AND MEDICINE

PROCEEDINGS

T.M.S. Chang, Chairman

C.R. Alving, Vice-Chairman

February 1983

(Conference dates July 12-16, 1982)

Supported by

US Army Medical Research and Development Command
Fort Detrick, Frederick, MD 21701

Grant No. DAMD17-82-G-9505

Gordon Research Conferences
University of Rhode Island
Kingston, RI 02881

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Report includes listing of participants and topics discussed at the Gordon Research Conference on Drug Carriers in Biology and Medicine, held July 12-16, 1982, at Plymouth State College-South, Plymouth, New Hampshire 03264.		

PROCEEDINGS OF GORDON RESEARCH CONFERENCEDRUG CARRIERS IN BIOLOGY AND MEDICINE

July 12-16, 1982

PLYMOUTH STATE COLLEGE-SOUTH, PLYMOUTH, N.H. 03264

Chairman; T.M.S. Chang, Vice-Chairman: C.R. Alving

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CONTENTS:Monday, July 12Artificial Cells as Carriers; T.M.S. Chang, Session Chairman

T.M.S. Chang, from Artificial Cells and Organs Research Centre, McGill University, 3655 Drummond Street, Montreal, PQ, Canada H3G 1Y6, started the session by introducing the areas of artificial cells as carriers.

A.P. Jarvis, Jr., from Damon Biotech., 115-4th Avenue, Needham Heights, MA 02194, then discussed their studies on microencapsulation of plasma cells for monoclonal antibodies production including methodology.

A.M. Sun, from Islet & Hormone Research, Connaught Research Institute, 1755 Steeles Ave. West, P.O. Box 1755, Station "A", Willowdale, ON, Canada M2R 3T4, discussed their research on implantation of microencapsulated islet cells in diabetic rats, demonstrating that this can control blood glucose for up to three months.

D. Terman, from Department of Medicine, Immunology, Baylor College of Medicine, Houston, TX 77030, discussed their successful preliminary clinical trials of plasma perfusion over protein A collodion charcoal for breast cancer and reviewed their clinical results.

T.M.S. Chang, from Artificial Cells and Organs Research Centre, McGill University, 3655 Drummond Street, Montreal, PQ, Canada H3G 1Y6, discussed two of the areas of research on artificial cells. The present status of artificial cells for the treatment of uremic patients has already reached the stage for large scale industrial production for large scale clinical trial. The use of artificial cells in liver failure has been analyzed in laboratory and animal studies.

Biological Cells as Carriers; G.M. Ihler, Session Chairman

G.M. Ihler, from Department of Medical Biochemistry, Texas A&M University, 110 Herman Heep Building, College Station, TX 77843, discussed their research on the potential uses of erythrocytes as carriers for drugs, enzymes and DNA with emphasis on studies on DNA for possible applications in genetic engineering.

R. Green, from Scripps Clinic and Research Foundation, 10666 North Torrey Pines Road, La Jolla, CA 92037, discussed their results obtained with red cell ghost for delivery of iron chelators.

U. Srandel, from Medical Polyclinic, University of Munich, PettenkoferstraBe 8a, D-8000 Munich 2, West Germany, discussed their work on the in vivo fate and effects of substances entrapped into erythrocyte ghosts.

Tuesday, July 13

Liposomes as Carriers, G. Gregoriadis, Session Chairman

G. Gregoriadis, from Medical Research Council, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, U.K., described their research on control of liposomes in-vivo.

C. Nicolau, from Recherche CNRS, Centre de Biophysique Moleculaire, Avenue de la Recherche Scientifique, 45045 Orleans Cedex, France, discussed the possibility and possible mechanisms of liposomes for gene-transfer in-vivo.

G. Poste, from Smith Kline & French Laboratories, 1500 Spring Garden Street, P.O. Box 7929, Philadelphia, PA 19101, described the possibilities of liposome immunomodulators in modifying host defense. He also discussed the possible problems related to this approach.

S.H. Kuhn, from Department of Internal Medicine, University of Stellenbosch, Faculty of Medicine, P.O. Box 63, Tygerberg 7505, South Africa, described his collaborative work with Finkelstein and Weissmann on interaction of liposomes with leukocytes.

Antibodies Complexed Carriers, D. Papahadjopoulos, Session Chairman

D. Papahadjopoulos, from Cancer Research Institute, University of California, Parnassus Str. M-1282, San Francisco, CA 94143, discussed the possibilities and laboratory results of antibody-liposome targeting.

I.J. Fidler, from NCI- Frederick Cancer Center, P.O. Box B, Frederick, MD 21701, discussed their studies on liposomes in macrophage activation and eradication.

M. Trudel, from Centre de Recherche en Virology, Institut Armand Frappier, 531 Boul. des Prairies, P.O. Box 100, Laval-des-Rapides, PQ, Canada H7V 1B7, discussed their experimental work on liposome adsorbed viral protein for vaccine. Their conclusion is that this is promising but further work is required.

Wednesday, July 14

Enzyme Therapy, R.O. Brady, Session Chairman

R.O. Brady, from Developmental and Metabolic Neurology Branch, National Institutes of Health, Building 10, Room #d04, Bethesda, MD 20805, discussed the different strategies for targeting exogenous enzymes for effective replacement therapy in metabolic disorder. Their studies have included the modifications of enzyme molecules for possible targeting.

M. Poznansky, from Department of Physiology, University of Alberta, Edmonton, AB, Canada T6G 2H7, discussed their research on soluble-enzyme albumin polymer demonstrating that this can prevent immunological reaction and continues to act effectively.

F.F. Davis, from Department of Biochemistry, Rutgers, State University of New Jersey, P.O. Box 1059, Piscataway, NJ 08854, discussed enzyme therapy using soluble enzyme-polyethylene glucol conjugates. They have carried out clinical trials which showed promising results.

R.A. Chalmers, from Medical Research Council, Clinical Research Centre, Division of Inherited Metabolic Diseases, Watford Road, Harrow, Middlesex HA1 3UJ, U.K., discussed and compared the potential of hypo-osmotic and iso-osmotic erythrocyte ghosts and carrier erythrocytes as drug and enzyme carriers.

Microcapsules and Microspheres in Experimental Therapy, M. Poznansky,
Session Chairman

D.L. Gardner, from Battelle Memorial Institute, 505 King Avenue, Columbus, OH 43201, discussed their studies on ingestible microencapsulated urease-zirconium phosphate for urea removal. Clinical trial has been initiated.

I. Sjöholm, from Uppsala Universitets, Biomedicinska Centrum, Institutionen for Farmaceutisk Biokemi, Biomedicum, Box 578, S-751 23 Uppsala, Sweden, discussed enzyme biodegradable microparticles in animal studies demonstrating effective in-vivo activities.

K.J. Widder, from Kendrew Biosystems, Inc., 11180 Roselle Street, Suite A, San Diego, CA 92121, discussed total remission in tumor-bearing rats treated with magnetically directed albumin microspheres. The tumors are implanted in the tails. Magnetic microspheres injected intraarterially in the tail are located by external magnetic field. This successfully suppressed tumor growth.

T. Kato, from Akita University, School of Medicine, Department of Urology, Akita 010, Japan, discussed target directed microcapsules for drug delivery for cancer therapy. They employed large microcapsules for local embolism to tumor site. Their large scale clinical results were promising.

Thursday, July 15

Carriers for Controlled Release, R.S. Langer, Session Chairman

R.S. Langer, from Biochemical Engineering, Massachusetts Institute of Technology, Department of Nutrition and Food Science, Cambridge, MA 02139, described a number of macroscopic implantable drug release systems.

P.J. Blackshear, from Massachusetts General Hospital, Diabetes Unit, Boston, MA 02114, described drug delivery systems by implantable pump, a number of possible applications were described and discussed.

F. Lim, from Department of Pathology, Medical College of Virginia, Virginia Commonwealth University, MCV Station, Richmond, VA 23298, described microencapsulated insulin for control release studies. This is an in-vitro study only, demonstrating the feasibility for slow release.

C. Hoff, from Laboratory of Medical Biochemistry, Rockefeller University, 1230 York Avenue, New York, NY 10021, described glucose dependent insulin delivery system in which insulin can be released in increasing amounts by increase in glucose concentration.

H.J.-P. Ryser, from Boston University Medical Center, School of Medicine, 80 East Concord Street, Boston, MA 02118, described polycationic drug-carriers for modulation of intracellular drug release - mechanisms of this approach were discussed in detail.

✓ Novel Carrier Systems, E.P. Goldberg, Session Chairman

E.P. Goldberg, from College of Engineering, Department of Materials Science MAE217, University of Florida, Gainesville, FL 32611, described tissue binding drugs for localized chemotherapy.

L.B. Wingard, from Department of Pharmacology, University of Pittsburgh, 620 Scaife Hall, Terrace and deSoto Streets, Pittsburgh, PA 15261, discussed immobilized anti-cancer drugs in cell surface action. This is an experimental approach where drug is immobilized to solid support. His result demonstrates a possible approach to analyze whether the drug being tested can carry out its action without entering the cells.

B. Erni, from Department of Microbiology Biocenter, University of Basel, Klingelbergstr. 77, CH-4056 Basel, Switzerland, described some very preliminary studies on lipid vesicles incorporated with cell membrane transport carriers extracted from cell membranes.

✓ Friday, July 16

✓ Liposomes in Therapy and Diagnosis, C.R. Alving, Session Chairman

C.R. Alving, from Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Washington, D.C. 20012, described their very successful results on the use of liposomes in leishmaniasis. During discussion, promising results on the use of liposomes in Malaria were summarized.

M.W. Fountain, from Liposome Company, 1-Research Way, Princeton Forrestal Center, Princeton, NJ 08540, described the successful use of liposomes in eradication of brucellosis in-vivo in animal studies.

W.E. Magee, from University of Idaho, Bacteriology/Biochemistry, Life Science Building, Room 14, Moscow, ID 83843, described the therapeutic efficacy of liposomes containing amphotericin B for fungal infections. These studies were carried out in animals.

V.J. Caride, from Hospital of St. Raphael, Yale University, Nuclear Medicine, 1450 Chapel Street, New Haven, CT 06511, discussed the possible use of liposomes in diagnostic imaging.

Closing Remarks

T.M.S. Chang thanked the speakers and session chairmen for their participation.

C.R. Alving, the 1984 Chairman of this Conference, discussed his general plan for the next conference.

GORDON RESEARCH CONFERENCES
DRUG CARRIERS IN BIOLOGY AND MEDICINE

JULY 12-16, 1982
PLYMOUTH STATE COLLEGE-SOUTH, PLYMOUTH, N.H. 03264

Chairman: T.M.S. Chang, Vice Chairman: C.R. Alving

Monday, July 12

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Artificial Cells as Carriers	T.M.S. Chang, Session Chairman McGill Univ.
Microencapsulation for monoclonal antibodies production	P.J. Vasington Damon Corp.
Implantation of microencapsulated islet cells in diabetic rats	A.M. Sun Connaught Res. Inst.
Plasma perfusion over protein A collo-dion charcoal for breast cancer	D. Terman Baylor College of Medicine
Biological Cells as Carriers	G.M. Ihler, Session Chairman Texas A&M Univ.
Potential uses of erythrocytes as carriers for drugs, enzymes and DNA	G.M. Ihler Texas A&M Univ.
Red cell ghost delivery of iron chelators	R. Green Scripps Clinic & Res. Found.
In vivo fate and effects of substances entrapped into erythrocytes	U. Sprandel Univ. Munich

Tuesday, July 13

Liposomes as Carriers	G. Gregoriadis, Session Chairman Med. Res. Council
Control of liposomes in-vivo	G. Gregoriadis Med. Res. Council
Liposomes for gene-transfer <u>in vivo</u>	C. Nicolau C.N.R.S.
Liposome immunomodulators in modifying host defense	G. Poste Smith Kline & French Labs.
Liposomes as carrier	M.C. Finkelstein N.Y. Med. College
Antibodies Complexed Carriers	D. Papahadjopoulos, Session Chairman CRI, UCSF
Antibody-liposome targeting	D. Papahadjopoulos CRI, UCSF

Drug Carriers

Transferring receptor as target for antibody-drug targeted therapy

I. Trowbridge
Salk Inst.

Can liposome adsorbed viral protein make an efficient vaccine?

M. Trudel

Wednesday, July 14

Carriers in Enzyme Therapy

R.O. Brady, Session Chairman
Nat. Inst. of Health

Strategies for targeting exogenous enzymes for effective replacement therapy in metabolic disorder

R.O. Brady
Nat. Inst. of Health

Soluble-enzyme albumin polymer

M. Poznansky
Univ. of Alberta

Enzyme therapy using soluble enzyme-polyethylene glycol conjugates

F.F. Davis
Rutgers Univ.

Erythrocyte entrapment for in-vivo enzyme delivery and immunologic protection

R.J. Desnick
Mt. Sinai School of Med.

Comparison and potential of hypo-osmotic and iso-osmotic erythrocyte ghosts and carrier erythrocytes as drug and enzyme carriers

R.A. Chalmers
M.R.C. Clinical Res. Ctr.

Microcapsules and Microspheres in Experimental Therapy

M. Poznansky, Session Chairman
Univ. of Alberta

Ingestable microencapsulated urease-zirconium phosphate for urea removal

D.L. Gardner
Battelle Memorial Inst.

Enzyme biodegradable microparticles in-vivo

I. Sjöholm
Swedish Nat. Board of Health

Total remission in tumor-bearing rats treated with magnetically directed albumin microspheres

K.J. Widder
Univ. California

Target directed microencapsules for drugs delivery

T. Kato
Akita Univ. School

Thursday, July 15

Carriers for Controlled Release

R.S. Langer, Session Chairman
MIT

Insulin delivery by macroscopic implantable pump

P.J. Blackshear
Mass. Gen. Hosp.

Microencapsulated insulin for control release studies

F. Lim
Med. College of Virginia

Glucose dependent insulin delivery system	C. Hoff Akzona
Polycationic drug-carriers: Modulation of intracellular drug release	H.J.-P. Ryser and W.-C. Shen Boston Univ. School of Med.
Novel Carrier Systems	E.P. Goldberg, Session Chairman Univ. of Florida
Tissue binding drugs for localized chemotherapy	E.P. Goldberg Univ. of Florida
Immobilized anticancer drugs in cell surface action	L.B. Wingard Univ. Pittsburgh Med. School
Artificial cells with reconstituted biological membrane	B. Erni Univ. of Basel
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Liposomes in leishmaniasis and malaria	C.R. Alving Walter Reed Army Inst. of Res.
→ <u>Liposomes in eradication of brucellosis in vivo</u>	M.W. Fountain Liposome Co.
Therapeutic efficacy of liposomes containing amphotericin B	W.E. Magee Univ. Idaho
Use of liposomes in diagnostic imaging	V.J. Caride Hosp. of St. Raphael
Liposomes in macrophage activation and eradication of metastasis	I.J. Fidler Fred. Cancer Res. Fac.
Closing Remarks	T.M.S. Chang McGill Univ. C.R. Alving Walter Reed Army Inst. of Res.

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